REMARKS

By Office Action mailed December 1, 2005, reconsideration of which is respectfully requested in view of the above amendments and following remarks. Claims 5, 6, 12, 15 and 17 have been amended as discussed in detail below, Claims 8 and 9 have been cancelled, and Claims 18 and 19 have been newly added. With the entry of this amendment, Claims 1-7 and 10-19 will be pending.

Prior Rejection of Claims 1-17 under 35 U.S.C. 102(b)

The Examiner found Applicants' arguments regarding the prior rejection of Claims 1-17 under 35 U.S.C. 102(b) in view of U.S. Patent No. 6,316,648 ("Serhan") to be persuasive and withdrew the rejection.

Rejection of Claims 6-17 under 35 U.S.C. § 112, ¶1

The Examiner newly rejected Claims 6-17 under 35 U.S.C. § 112, ¶1, for lack of enablement. In particular, the Examiner contended that:

> *. . .the specification, while being enabling for the treatment of asthma and the inflammatory response does not reasonably provide enablement for treating or preventing of the other various diseases listed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.*
>
> *While linear lipoxin analogs may be known in the art to treat various diseases, there is no evidence that these same characteristics have been attributed to the instant benzo-lipoxin analogues. Applicants have not shown that the other various diseases listed can be treated using the instant compounds; there is no apparent correlation that all of the listed diseases can be treated using the same compounds. Also there is no correlation that these compounds when given can prevent mammals from getting these diseases.*

Claim 6 has been amended to remove the phrase "useful in treating an inflammatory or autoimmune disorder in a mammal", thereby rendering moot this rejection with respect to Claims 6 and 7.

Claims 8 and 9 have been cancelled in favor of amended Claim 6 and 7, thereby rendering moot this rejection with respect to Claims 8 and 9.

Applicants traverse this rejection with respect to Claims 10-17 for the following reasons.

Lipoxin A_4 and lipoxin A_4 analogs are known anti-inflammatory agents. For example, the Examiner's attention is directed to Takano, T. et al., "Neutrophil-mediated Changes in Vascular Permeability Are Inhibited by Topical Application of Aspirin-triggered 15-epi-lipoxin A_4 and Novel Lipoxin B_4 Stable Analogues," *Journal of Clinical Investigation 101*: 819-826, 1998, and Serhan, C. et al., "Design of Lipoxin A_4 Stable Analogs That Block Transmigration and Adhesion of Human Neutrophils," *Biochemistry 34*: 14609-14615, 1995, copies of which were submitted with the Information Disclosure Statement filed September 27, 2004. These journal references discuss lipoxin A_4 and lipoxin A_4 analogs and their anti-inflammatory and immunomodulatory activity.

Rejected Claims 10-17 are directed to methods of treating inflammatory disorders, autoimmune disorders, pulmonary inflammation or respiratory tract inflammation by administering the compounds of the invention to a subject in need thereof. One of ordinary skill in the art would reasonably expect that the compounds of the invention, in being lipoxin A_4 analogs, would be useful in treating such disorders and inflammation, particularly those disorders which are mediated by neutrophils, eosinophils, T lymphocytes, NK cells or other immunomodulatory cells which contribute to the pathogenesis of inflammatory, immune or autoimmune diseases. All of the inflammatory or autoimmune disorders specifically recited in Claims 12 and 15-17 are known as being mediated by neutrophils, eosinophils, T lymphocytes,

NK cells or other immunomodulatory cells. Thus, one of ordinary skill in the art would also reasonably expect that the compounds of the invention would be useful in treating the specific disorders recited in Claims 12 and 15-17.

Furthermore, one of ordinary skill in the art would need to look no further than the Specification in determining how to test the compounds of the invention for the claimed use. The Specification provides ample disclosure on pages 17-18 as to standard *in vitro* and *in vivo* assays which one could employ to test the compounds' ability to act as an anti-inflammatory or immunomodulating agent. Furthermore, Examples 11-14 provide specific teachings as to standard *in vitro assay* and *in vivo* assays which were used to test the compounds' abilities as anti-inflammatory or immunomodulating agents. Thus, Applicants respectfully submit that, contrary to the Examiner's contention, the Specification clearly provides sufficient teaching to enable one skilled in the art to use the compounds in treating the disorders as set forth in Claims 10-17.

Applicants respectfully submit that the Examiner has not provided any objective evidence that would contradict this conclusion. As the USPTO's Training Materials for Examining Patent Applicants with respect to 35 U.S.C. 112 Section 112, First Paragraph - Enablement Chemical/Biotechnical Applications ("Training Materials") states:

> *It is proper to accept as being true the statement that the [compounds] were active in the assays, even in the absence of specific data. The Office must accept as being true the statements supporting enablement unless there is an objective reason, usually supported with documentary evidence, to question them, i.e., the burden is on the Office to demonstrate that there is an objective reason, usually supported by documentary evidence, to question the statement.*

Applicants note that the Specification specifically states that the compounds of the invention were active in each of the assays tested. As noted above, the assays disclosed in the Specification are known assays used to test the anti-inflammatory or immunomodulating activity of a compound. Accordingly, since the Examiner has not provided any evidence that would

question these statements, Applicants respectfully submit that the Examiner must accept as being true that the compounds are indeed active in the assays specifically disclosed in the Specification in Examples 11-14.

Applicants submit that it would appear that the Examiner, in making this rejection, is arbitrarily imposing a requirement whereby, in order to obtain patent protection of the methods of use claims under 35 U.S.C. 112, ¶1, Applicants must test each claimed compound for its ability to treat a subject for each disorder specifically listed in Claims 12 and 15-17. Such a requirement would clearly be prohibitive for the Applicants in terms of time and money and is not required by current patent law. As the court in *In re Brana*, 34 USPQ2nd 1436 stated:

> *Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The state at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing [i.e., effectiveness in humans] in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas. . . .*

Accordingly, in view of the extensive teaching of the specification with respect to the *in vitro* and *in vivo* assays which one can use to test the claimed compounds' ability to act as an anti-inflammatory or immunomodulating agent, and in view of the lack of evidence provided by the Examiner to substantiate the Examiner's contention that the invention is not enabled, Applicants respectfully submit that the pending method of use claims, *i.e.*, Claims 10-17, satisfy the enablement requirement of §112 and respectfully request that this ground of rejection be withdrawn.

In addition, for the same reasons, Applicants respectfully submit that newly added Claims 18 and 19 are fully enabled by the Specification as originally filed.

Applicants submit herewith, in a Supplemental Information Disclosure Statement, the following references:

Guilford, W.J. *et al.*, "Second-generation beta-oxidation resistant 3-oxa-lipoxin A4 analogs", *Prostaglandins Leukot. Essent Fatty Acids* (2005), Sept-Oct; 73/3-4:245-50;

Fiorucci, S. *et al.*, "A beta-oxidation-resistant lipoxin A4 analog treats hapten-induced colitis by attenuating inflammation and immune dysfunction", *Proc. Natl. Acad. Sci. U.S.A.* (2004), Nov 2;101(44):15736-41;

Bannenberg, G. *et al.*, "Lipoxins and novel 15-epi-lipoxin analogs display potent anti-inflammatory actions after oral administration," *Br. J. Pharmacol.* (2004), Sep;143(1):43-52; and

Guilford, W.J. *et al.*, "Novel 3-oxa lipoxin A4 analogues with enhanced chemical and metabolic stability have anti-inflammatory activity in vivo", *J. Med. Chem.* (2004), Apr 8;47(8):2157-65.

These references, which disclose the claimed compounds and their use as anti-inflammatory or immunomodulating agents, further support the use of the claimed compounds as set forth in Claims 10-17.

Rejection of Claims 5, 12, 15-17 under 35 U.S.C. § 112, ¶2

The Examiner rejected Claims 5, 12, and 15-17 under 35 U.S.C. § 112, ¶2, for indefiniteness. In particular, the Examiner contended that Claims 5, 12, and 15-17 contain improper Markush language and referenced MPEP section 2173.05(h), page 2100-700 for support.

In a telephonic interview with the Examiner on January 26, 2006, with the undersigned attorney, the Examiner indicated that the improper Markush language was the phrase "the following". Applicants have amended Claims 5, 12 and 15-17 to remove this phrase.

Accordingly, Applicants respectfully request the withdrawal of this rejection of Claims 5, 12 and 15-17 under 35 U.S.C. § 112, ¶2.

Allowance of Claims 1-4

Applicants acknowledge the allowance of Claims 1-4.

Conclusion

Applicants respectfully submit that, in view of the above amendments and remarks, Claims 6-7 and 10-19 are clearly patentable under 35 U.S.C. § 112, and respectfully request their allowance at an early date.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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